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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/777,732	02/06/2001	Yingyos Avihingsanon	01948-059001	8709

26161 7590 11/19/2003

FISH & RICHARDSON PC
225 FRANKLIN ST
BOSTON, MA 02110

EXAMINER

TUNG, JOYCE

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 11/19/2003 .

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/777,732	AVIHINGSANON ET AL.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5,8,9 and 35-42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5,8,9 and 35-42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Following entry the amendment filed 9/2/2003, the claims 1-5, 8-9 and 35-42 are pending.

1. The response argues that Sores et al. et al. studied the cellular mechanisms that underlie transplant rejection and nothing in Soares' publication suggests that one should examine the expression of HO-1 in order to monitor the status of a transplanted organ and the expression data to predict the likelihood of graft rejection. However, the newly supplied reference of Strom et al. (6,187,534, issued 2/13/2001) discloses a method of evaluating transplant rejection in a host comprising determining a heightened magnitude of gene expression of immune activation marker gene in a tissue biopsy or peripheral blood mononuclear cell sample (See the Abstract). Thus, Applicant's arguments with respect to the rejection of claims 1-11 have been considered but are moot in view of the new ground(s) of rejection as set forth as follows.

New Grounds of Rejections

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-5 and 8-9 and 35-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strom et al. (6,187,534, issued 2/13/2001) in view of Soares et al. (Nature Medicine, 1998, Vol. 4(9), pg. 1073-1077).

Strom et al. disclose a method of evaluating transplant rejection in a host comprising determining a heightened magnitude of gene expression of immune activation marker gene in a tissue biopsy or peripheral blood mononuclear cell sample (See the Abstract). The method also relates to monitor the status of a transplanted organ in a host (See column 1, lines 22-23). The organ is kidney from human (See column 1, lines 39-42). The sample is from post-transplantation (See column 1, lines 43-46). The magnitude of the gene expression of the immune activation marker gene is determined by using competitive reverse transcription to quantify the gene transcripts (See column 1, lines 53-67 to column 2, lines 1-19 and column 2, lines 28-41). The constitutively expressed gene is glyceraldehyde-3-phosphate dehydrogenase and actin (See column 2, lines 7-11).

Strom et al. do not disclose determining the magnitude of gene expression of gene, heme oxygenase 1 (HO1) or A20 for monitoring the status of a transplanted organ in a host.

Soares et al. disclose that the expression of the heme oxygenase-1 (HO-1) is functionally associated with xenograft survival and that rapid expression of HO-1 in cardiac xenografts can be essential to ensure long-term xenograft survival (See pg. 1073, the Abstract). The gene expression of HO-1 is also determined by immunocytochemistry and by reverse transcriptase polymerase chain reaction (See pg. 1073, column 1, first paragraph). Expression of the gene,

HO-1 was also detected in xenograft undergoing rejection (See pg. 1073, column 2, first paragraph). Soares et al. also disclose that to determine whether HO-1 expression was functionally associated with xenograft survival, the graft survival was assessed every 10-12 hours (See pg. 1073, column 2, second paragraph) and that overexpression of HO-1 or the anti-apoptotic gene A20 is to suppress apoptosis (See pg. 1074, column 1, second paragraph). The gene, HO-1 expression with the treatment of CyA and CVF was detected by reverse transcriptase polymerase chain reaction within 12-24 hours and 48-72 hours after transplant (See pg. 1074, column 2, last paragraph to pg. 1075, column 1, first paragraph).

One of ordinary skill in the art at the time of the instant invention would have been motivated to modify the method of Strom et al. to evaluate acute transplant rejection in a host by determining the magnitude of the expression of the gene, HO-1 or A20. Although Strom et al. do not explicitly disclose monitoring the status of a transplanted organ in a host by determining the magnitude of the expression of the gene, HO-1 or A20, Soares et al. studied the gene expression of HO-1 and A20 at different period time after transplantation and Soares et al. indicate that the gene, HO-1 expression was functionally associated with xenograft survival (See pg. 1073, column 2, second paragraph). Therefore, one of ordinary skill in the art at the time of the instant invention would have been motivated to apply the method of Strom et al. to evaluate acute transplant rejection in a host by determining the magnitude of the expression of the gene, HO-1 or A20. It would have been prima facie obvious to monitor the status of a transplanted organ in a host by determining the magnitude of the gene expression of the gene, HO-1 or A20.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-5, 8-9 and 35-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-5, 8-9 and 35-42 are vague and indefinite because the preamble states that the method is for monitoring the status of a transplanted organ in a host, but there is no monitoring step in the method step. Clarification is required.

Summary


6. No claims are allowable


7. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

8. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung 
November 5, 2003


JEFFREY SIEW
PRIMARY EXAMINER